**Potent PPARα-agonist**

PPAR subtype selectivity (α, γ, δ)

- Ligand-specific binding and affinity
  - NR conformational change
  - Co-activator recruitment
  - Ligand-specific gene expression pattern
  - Increase / decrease or quenching of outcome effects

**PPARα-agonist molecular mechanism**

**PPARα-agonist clinical effects**

- Efficacy:
  - TG and cholesterol (↓)
  - HDL and Apo A1 (↑)
  - FGF-21 (↑)

- Side effects:
  - ALT/γ GT (liver)
  - Homocysteine (cardiovascular)
  - Creatinine (kidney)

**SPPARMα clinical benefits vs comparable doses of fenofibrate**

- Greater efficacy:
  - TG and cholesterol (↓)
  - HDL and Apo A1 (↑)
  - FGF-21 (↑)

- Reduced side effects:
  - ALT/γ GT (liver)
  - Homocysteine
  - Creatinine

**SPPARMα-therapeutic potential**

- Micro and macrovascular disease
- NASH / NAFLD